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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/502,283	02/11/2000	Sun Ai Raillard	02-02951BUS	4948

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EXAMINER
FRIEND, TOMAS H F

ART UNIT	PAPER NUMBER
1627	

DATE MAILED: 09/23/2002 18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/502,283	RAILLARD ET AL.	
	Examin r	Art Unit	
	Tomas Friend	1627	

file copy

-- The MAILING DATE of this communication appears on the cover she t with th c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-80* is/are pending in the application.

4a) Of the above claim(s) *27-71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21,72-78 and 80* is/are rejected.

7)☒ Claim(s) *22-26 and 79* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *13* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

Status of the Application

Receipt is acknowledged of a response to an office action (with amendment and I.D.S.) and a change of address on 11 June 2002 (Paper Nos. 15 and 16).

Status of the Claims

Claims 1-71 were pending in the present application. Claims 27-71 were withdrawn from further consideration in Paper No. 12. New claims 72-80 were added in Paper No. 15.

Claims 1-26 and 72-80 are pending and examined on their merits.

Withdrawal of Allowability

The indicated allowability of claims 18-21 is withdrawn in view of the newly discovered reference(s) to Little et al. U.S. Patent 6,322,970 B1 November 2001 (filed 02 September 1998). Rejections based on the newly cited reference(s) follow.

Information Disclosure Statements

All references listed in the three information disclosure statements submitted have been located and considered by the examiner. It is noted that more than 100 references disclosed were not accompanied by any comment or discussion concerning the relevancy of the listed patents and printed publications. The examiner, therefore, has considered these references to the extent possible, given the time available for examination.

Withdrawn Rejections/Objections

1. The rejection of claim 1 under 35 U.S.C. 112, second paragraph, over "*an off-line parallel adjustment of cell growing conditions*" is withdrawn in response to applicants' amendment.

2. The rejection of claim 1 under 35 U.S.C. 112, second paragraph, over column separation being excluded entirely from the method is withdrawn in response to applicants' amendment.

3. The rejection of claim 1 under 35 U.S.C. 112, second paragraph, over "performing flow–injection analysis using electrospray tandem mass spectrometry" is withdrawn in response to applicants' argument.

4. The rejection of claim 2 under 35 U.S.C. 112, second paragraph, is withdrawn in response to applicants' amendment.

5. The rejection of claims 3-7 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps is withdrawn in response to applicants' amendment.

6. The rejection of claims 5 and 6 under 35 U.S.C. 112, second paragraph, over mixed broad and narrow ranges is withdrawn in response to applicants' amendment.

7. The rejection of claims 1 and 12-17 under 35 U.S.C. 102(e) as being anticipated by Chace U.S. Patent 6,258,605 B1 is withdrawn in response to applicants' amendment.

8. The objections to claims 18-21 made in Paper No. 12 are withdrawn.

Maintained Rejections/Objections

The statutory basis for each of the following rejections may be found in a prior office action.

Maintained Objections

9. Claims 22-26 remain objected and new claim 79 is objected to for depending from rejected claims.

Maintained Rejections – 35 U.S.C. 112, second paragraph

10. Claim 1 and newly amended claim 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 remains rejected and newly amended claim 18 is rejected over the metes and bounds of the term "*component.*" Applicants argue that the term is defined in the specification on, for example, page 5, lines 2-11. Applicants' argument has been carefully considered and found not to be persuasive because the list on page 5 of what may be included by the term "component" is open ended and preceded by the term "optionally."

New Grounds of Rejection

The statutory basis for each of the following rejections not found below may be found in a prior office action.

New Grounds of Rejection - 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claim 76 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (New Mater).

It appears that there is no support in the specification for the newly added claim which recites the limitation "*wherein the off-line parallel purification system comprises solid phase extraction.*" In accordance with MPEP 714.02, applicant may overcome this rejection by specifically pointing out where support can be found for this amendment.

New Grounds of Rejection – 35 U.S.C. 112, second paragraph

12. Claims 3-6, 13, 21, and 76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 3-6 recite the limitation "*cell colonies.*" There is insufficient antecedent basis for this limitation in the claims.

B. In claim 13, it is not clear how non-column-separated components can be generated from reactions of purified cell enzymes with added substrates because this creates a component that was not purified from a cell but created using components from a cell, which appears to be outside the scope of claim 1 from which claim 13 depends. Method step (iii) of claim 1 recites "*injecting the sample containing one or more non-column-separated component into a mass spectrometer.*"

C. Claim 21 depends from claim 19, which has been amended to depend from claim 18. Claim 21 recites "*performing flow injection analysis on one or more product*" (of contacting the library of enzymes with one or more substrates). Claim 18 recites "*injecting the sample containing the one or more non-column-separated component into a mass spectrometer*" and "*performing flow-injection analysis ...on the one or more non-column-separated component from the one or more cell...*" It appears that claim 21 is reciting a method in which a sample comprising product produced using a non-column-separated component is injected into a mass

spectrometer rather than a sample comprising the non-column-separated component as required by claim 18. Clarification is requested.

D. In claim 76, the metes and bounds of the term "*solid phase extraction*" are not clear.

New Grounds of Rejection – 35 U.S.C. 102

13. Claims 1, 12-20, 75, and 76 are rejected under 35 U.S.C. 102(e) as being anticipated by Little et al. U.S. Patent 6,322,970 B1 November 2001 (filed 02 September 1998).

The Little et al. patent discloses a method for determining the identity of a target polypeptide using mass spectrometry (abstract). Column 3, line 66 to column 4, line 13, discloses that the mass spectrometric analysis used includes continuous electrospray ionization (i.e. flow-injection analysis). Column 3, lines 55-65, discloses that a target polypeptide including polyhistidine, polylysine, or polyarginine tags can be produced by transformed bacterial or transfected mammalian cells (i.e. one or more cells grown in vitro). Column 4, lines 43-65, discloses that the target polypeptide (i.e. component) is generally isolated (purified) prior to MS analysis. Column 9, lines 46-56, discloses the use of at least one of molecular mass or charge to determine the identity of a target polypeptide. Column 5, lines 18-21 and column 7, lines 51-57, disclose that target polypeptides may be immobilized as addressable arrays on silicone wafers or microchips. Accordingly, the Little et al. patent anticipates present claims 1, 13, 14, 17, and 76.

Column 10, lines 33-39, discloses the use of cation exchange resin to condition (i.e. purify) target polypeptides, anticipating present claim 12. Column 9, lines 31-45, discloses that a polypeptide may be enzymatically modified (i.e. a substrate for an enzyme), anticipating present claim 15. Column 73 discloses a polypeptide with hydrophobic residues (hydrophobic moieties), anticipating present claim 16. Column 15, line 60, to column 16, line 14, discloses that target polypeptides may be immobilized in solid supports that have features including pins, beads, and wells, anticipating present claim 18. Column 7, lines7-12 lists specific disease-related target polypeptides including enzymes, anticipating present claim 19. Column 15, lines 16-45, discloses the use of biotin, avidin, and streptavidin to immobilize target polypeptides on a solid

support, anticipating present claim 20. Column 6, lines 27-31, discloses a kit that includes organic solvent for volatilizing and ionizing the target polypeptide, anticipating present claim 75.

New Grounds of Rejection – 35 U.S.C. 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 1-20, 72-78, and 80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Little et al. U.S. Patent 6,322,970 B1.

The Little et al. patent teaches a method for determining the identity of a target polypeptide using mass spectrometry including continuous electrospray ionization (i.e. flow-injection analysis). Target polypeptides including polyhistidine, polylysine, polyarginine, or biotin tags can be produced by transformed bacterial or transfected mammalian cells (i.e. one or more cells grown in vitro). Target polypeptides (i.e. components) are generally isolated (purified) prior to MS analysis using at least one of molecular mass or charge to determine the identity of a target polypeptide. Target polypeptides may be immobilized as addressable arrays on silicone wafers, microchips, pins, beads, and wells, or conditioned with cation exchange resin and/or organic solvent. A target polypeptide may be enzymatically modified (i.e. a substrate for an enzyme), and may include hydrophobic residues (hydrophobic moieties). Accordingly, claims 1, 12-20, 75, and 76 are unpatentable over the Little et al. patent. For a more detailed analysis of the Little et al. reference please see the rejection under 35 U.S.C. 102.

The Little et al. patent does not explicitly teach:

[1] that cells are alive during target peptide conditioning (i.e. purification),

[2] time required to identify target polypeptides from a particular number of cells (colonies),

[3] using a particular number of cells or cell colonies concurrently,

[4] centrifugation or filtration of cells to condition a target polypeptide,

[5] using an automated sampler to transport samples,

[6] pooling of target peptides before MS, or

[7] neutral loss and parent ion MS.

With respect to [1], it would have been obvious to one of ordinary skill in the art at the time that the invention was made to keep cells alive during target peptide conditioning. One would have been motivated to do so in cases of secreted target polypeptides because killing the cells before contacting the growth media with a tag-binding solid support would be an unneeded additional step. Accordingly, claim 2 is unpatentable over Little et al.

With respect to [2, 3, 5, and 6], it would have been obvious to one of ordinary skill in the art at the time that the invention was made to optimize the method to minimize the time required. Column 7, lines 51-67, teaches the immobilization of up to 9,999 or more target polypeptides on a single solid support and using a multiplexing format in which multiple target polypeptides can be identified simultaneously. This suggests/teaches that reducing screening time is desirable. One of ordinary skill in the art would reasonable expect that the combined use of solid support arrays and multiplexing would successfully identify (screen) 500 cells (grown simultaneously) in less than an hour or 1000 cells in less than a day. Additionally, the use an automated sampler and pooling of samples would be obvious methods of reducing screening time because automated samplers were routinely in use at the time and pooling of samples would be suggested by the multiplexing format. Accordingly, claims 3-11, 77, and 78 are unpatentable over Little et al.

With respect to [4], it would have been obvious to one of ordinary skill in the art at the time that the invention was made to centrifuge or filter cells to separate then from the supernatant medium because these are commonly used separation techniques that concentrate cells for further purification of cellular polypeptides and remove cells from the medium for purification of secreted polypeptides. Accordingly, claims 72 and 73 are unpatentable over Little et al.

With respect to [7], it would have been well within the abilities of one of ordinary skill in the art at the time that the invention was made to perform neutral loss and/or parent ion MS according to preference and/or need based upon experimental criteria such as the target polypeptides to be identified because both methods of MS were in routine use at the time that the invention was made. Accordingly, claims 23 and 80 are unpatentable over Little et al.

Allowable Subject Matter

15. Claims 22-26 and 79 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Tomas Friend** at telephone number **(703) 308-4548**. The examiner can normally be reached on Monday, Tuesday, Friday, and Saturday 8:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-2742.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist at (703) 308-1235.

Tomas Friend, Ph.D.
17 September 2002

PADMASHRI PONNALURI
PRIMARY EXAMINER